Article Info
Citation: Health by Numbers Portugal 2014; 2; 50-58
History: received - 22/5/2013
revised - 12/7/2013
accepted - 1/10/2013
proof revision - 14/10/2014
online - 24/11/2014

2014 november
number 02
health by numbers Portugal
Directorate General of Health Journal

English Version

D Was it possible to anticipate the intensity of the Madeira's dengue epidemic for the year 2013?

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Abstract: The dengue virus has had a detrimental effect on the inhabitants of many tropical areas, infecting millions of people worldwide. The dengue epidemic in the Autonomous Region of Madeira, a Portuguese archipelago, was officially declared by the Portuguese Health Authorities on the 3rd October, 2012.

The main objectives of this study were: **1)** to better understand the evolution of the dengue fever in Madeira and **2)** to anticipate possible scenarios for the year of 2013. This study was more challenging due to the absence of past evidence because it referes to the first epidemic of this kind on the island. Therefore, past information regarding outbreaks of this epidemic in other parts of the world was gathered to trace the behavior of the virus itself. Then, six regions of the world were selected according to predefined criteria that reflected similar ambient conditions to those of Madeira during the spread of the epidemic. It was concluded that in 2013, between **2160 and 2470 dengue clinical cases** were expected to occur in the archipelago. Up until the 3rd of February of 2013, a total of 2164 clinical cases were in Madeira.

Keywords: **dengue epidemic, dengue virus, attack rate, mortality rate, population density, subtropical climate**

1 Introduction

Dengue is a disease caused by a virus, DENV, and it is transmitted to a person through bites from the *Aedes Aegypti* mosquito, which generally breeds in big water containers. However, dengue can also be transmitted by the species *Aedes albopictus*, which breeds in small containers, such as flowerpots. The big urban centers have been the most convenient places for these mosquitoes to find their principal source of food: human blood. The disease is prevailing in the southeast regions of Asia and recently has become more and more common in the tropical countries of the Pacific, Oriental Africa and Latin America[1]. As dengue viruses infect millions of people each year, this disease is considered to be one of the most important infectious diseases in many tropical and subtropical countries. In fact, research indicates that about 40% of the world's population lives in countries at risk of dengue infection[1].

Although cyclic, the incidence of this disease is increasing and spreading geographically[2]. There can be many causes for such a trend: for instance, an increase of the reported data, improved diagnostic tools, along with higher levels of urbanization. The tendency of countries becoming increasingly urbanized is clear, and with mosquitoes thriving in large cities, this could lead to a greater concentration of insects and hence a growth in dengue incidence. On the other hand, technologies, allowing a more efficient report of data, improved over time. Obviously, with more data reported, there will be better knowledge of dengue cases occurrence.

The dengue virus' incubation period is about 3-7 days, but it can last up to two weeks [1]. The virus can cause different symptoms on the humans. Usually it is flu-like, but in severe cases it can lead to death.

Theoretically, the number of people infected by the virus is expected to increase during periods characterized by extreme heat, substantial precipitation and relative humidity. These are the perfect conditions for the mosquito (host) to reproduce. Still, it should be taken into account that the rainfall cannot be too high, otherwise it may flood the breeding niches.

The Autonomous Region of Madeira is a Portuguese archipelago, with 267 785 inhabitants (2011)[3], located 520 km from the African Coast and 1,000 km from the Continental Europe. Madeira has an *infant mortality* rate of 3.4 per thousand[4], a *population density* of 300/km^2[5] and an *urban population* of about 70%. This last value is related to the most populated cities of Madeira: Funchal, Santa Cruz and Câmara de Lobos (contributing to a total of 0.19 million inhabitants[6]). The archipelago's subtropical climate is influenced by its geographical position, although there are clear weather variations between the northern and the southern regions. Madeira has a microclimate with average temperatures rarely falling outside the range of 13°C – 25°C. The hottest months are August and September, while the four month period between November and February has the highest average of rainfall (*Figures 1*[7], [8] and *2*[7], [8]).

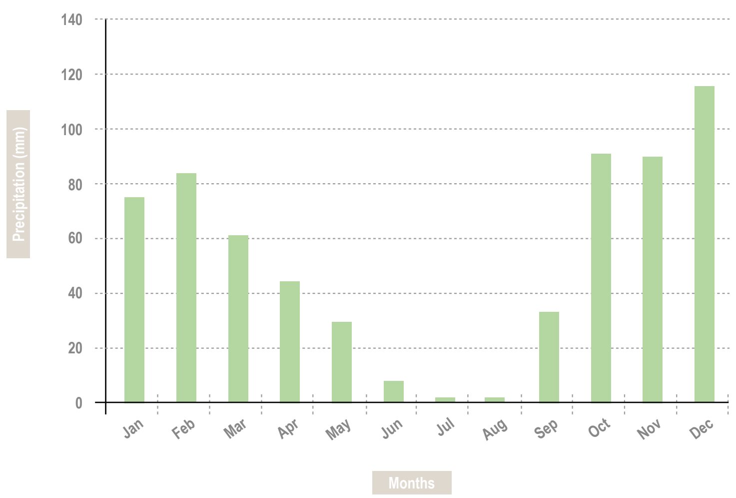
Figure:

1 Minimum and maximum average temperatures (°C) in Funchal (Madeira) for each month of the year

Source: http://www.weatheronline.co.uk[8]

Figure:

2 Precipitation (mm), in Funchal (Madeira), for each month of the year

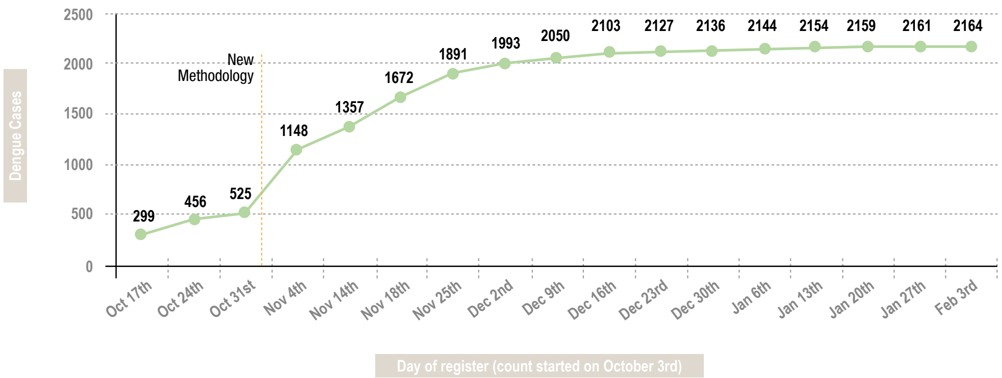


Source: http://www.weatheronline.co.uk[8]

The mosquito *Aedes Aegypti* was first identified in Madeira back in 2005, in the city of Funchal, and the dengue epidemic was officially declared by the Portuguese Health Authorities on the 3rd October of 2012 with two dengue confirmed cases. The evolution of Madeira's dengue fever, by week, is represented in *Figure 3*[9], with the rate of dengue incidence decreasing throughout this time period.

Figure:

③ Cumulative evolution of the dengue fever in Madeira, from the 3rd of October (2012) to the 3rd of February (2013)



Source: Directorate-General of Health. New methodology - refers to alteration of case definition made by guidelines update (10)

Dengue cases can be classified as probable or confirmed. A case is considered probable when it meets both clinical and epidemiological criteria. A clinical criterion is characterized by fever and two or more of the following symptoms: headache, retro-orbital pain, myalgia, arthralgia, exanthema, hemorrhagic manifestations or leucopoenia. The epidemiological criterion is present when a person lives in or has been in the dengue affected area within a period of 21 days from the onset of symptoms. A confirmed case appears with one or more of the following laboratory results: i) the presence of dengue-virus-specific IgM antibodies in the blood or in the cerebrospinal fluid; ii) a significant increase in the concentration of dengue-virus-specific IgG antibodies, or; iii) the detection of the dengue virus' nucleic acid in blood[11].

Through this work, a greater understanding of the factors contributing to the dengue outbreak can be achieved, thus allowing health care planning better suited to the needs of the Madeira population.

The goal of this study was to better understand the evolution of the dengue fever in Madeira, attempting to anticipate its trend for the rest of the year 2013. For this, it was not possible to use past information as Madeira is experiencing a dengue epidemic for the first time.

2 Methods

Being the first dengue epidemic in the archipelago of Madeira, there was no information about the disease to study its future evolution. Thus, information regarding outbreaks of this epidemic in other parts of the world was gathered to trace the behavior of the virus itself and to compare it to the case of Madeira. The selection of the countries followed some criteria to allow comparison with Madeira. Therefore, regions similar to Madeira were chosen, in terms of the conditions that are considered to foster the spread of dengue, namely the climate and the level of development.

For the first condition, countries with tropical and sub-tropical climates were chosen, with minimum and maximum temperatures of 15°C and 34°C, respectively. Countries with minimum average temperatures above 21°C were automatically excluded. At last, using this selection criterion, countries which had approximately the same number of rainy months as Madeira were selected.

The second condition, the level of development of a country, can often be evaluated through the following indicators: *infant* *mortality rate, urban population percentage and population density.* Hence, considering Madeira's profile, this criterion would only include countries with an *infant mortality* rate less than or equal to 16 per million, a *percentage of urban population* between 60% and 90% and a *population density* between 100/km^2 and 450/km^2. Overall, this criterion cannot be too strict, as it is difficult for the countries to fulfill all of the requirements. Candidate countries were those which had previous dengue outbreaks. Afterwards, they were selected according to the criteria described above with a focus on those which fulfilled as many of the above requirements as possible.

The six countries selected were: Cuba, The Bahamas, Guadeloupe, Vietnam (in particular South Vietnam), Australia (in particular Queensland) and Puerto Rico.

After, it was given a deep look at their dengue trend along the history, especially at the first outbreak because Madeira is experiencing that same situation as well. When the information was only available in terms of absolute figures, the *attack rates* were estimated using the formula:

$$\text{attack rates} = \frac{\text{number of dengue cases}}{\text{total population}} * 100$$

However, these *attack rates* refer to the total population of the country. Thus, as the mosquito of dengue chooses preferably urban zones, the attack rate referring to the *urban population* was also estimated:

$$\text{urban attack rates} = \frac{\text{number of dengue cases}}{\text{total population} * \%\ \text{urban population}} * 100$$

It is also important to note whether those *attack rates* refer to the probable cases or to the laboratory-confirmed cases because the analysis has credibility only if one compares the same type of indicators. The frequency and the duration of the outbreaks were also registered and, whenever possible, the serotypes were identified.

After gathering the information about all of the dengue outbreaks, it was noticed that some of them happened a long time ago and, of course, the conditions of the countries were not exactly the same at that time. Hence, more information relative to those past decades was obtained to see if the countries, during those years, would compare to current Madeira.

3

Results

A total of six countries were selected: Cuba, The Bahamas, Guadeloupe, Vietnam (in particular South Vietnam), Australia (in particular Queensland) and Puerto Rico. They all have tropical or subtropical climates and their minimum and maximum temperatures do not exceed the interval from 15°C to 34°C, respectively. Furthermore, recall that Madeira has four particularly rainy months and so the selected countries have between four to seven months of high rainfall. In terms of *infant mortality* rate, all the countries have less than 16 per million, highlighting that the lowest and the highest cases are 3.9 per million in Australia (2011) and 15.8 per million in The Bahamas (2003), respectively. There is an exception in the case of Vietnam, year 2002: 30 per million. Regarding to the population, The Bahamas, Guadeloupe, Puerto Rico and Australia-Queensland, with between 0.3 and 4.5 million inhabitants, were the most similar to Madeira, which has 0.4 million inhabitants. On the other hand, the *population density* varies between 166/km^2 and 436/km^2, for Cuba (2002) and Guadeloupe (2002), respectively. Concerning to the *urban population*, its percentage varied between 66% in Cuba (1977) and 100% in The Bahamas (2011). Once again, Vietnam does not fulfill the requirement and the same goes for Guadeloupe. These countries present values of approximately 17% (1975), 24% (2002) and 28% (2009) for Vietnam and 48% (2002) for Guadeloupe. All the results are shown in *Table 1*.

Table:

1 Resume of some of the characteristics of the six selected countries

Description of the Countries					
Country	Climate Min – Max Temp (°C) Rainy season **	Mortality Infant Rate (per million)*	Population (per million)*	Population density (/km2)*	Urban population (%)*
Cuba	Tropical 21°C-31°C (13) May to October	**6** (2002)	**9,6** (1977) (16) **11,3** (2002)	**166** (2002)	**66** (1977)(22) **75** (2002)
Guadeloupe	Subtropical tempered 20ºC-31°C July to November	**8,4** (2002) **6** (2009)	**0,4** (2002, 2005, 2009)	**436** (2002) **240** (2009)	**48** (2002) **100** (2011)
Puerto Rico	Tropical marine, mild 20°C-31°C April to November (14)	**10,6** (2002)	**2,3** (1963) (17) **3,9** (2002)	**698** (2002)	**48,7** (1963)(23) **67,4** (1981)(23) **95,8** (2002)(23)
Bahamas	Tropical Marine 15°C-31°C June to October	**15,8** (2003) **12** (2011)	**0,3** (2003) **0,4** (2011)	**36** (2003) **26** (2011)	**84** (2003, 2011)
Austrália	Tropical temperate 15°C-29°C (15) December to May[(15)	**5,2** (2009) **3,9** (2011)	**13,5** (1992) (18) **19,7** (2002) **22,7** (2011) **Queensland: 3** (1992) (19) **4** (2007-2010) (19) **4,5** (2011) (19)	**4** (2002) **3** (2011)	**85** (2002) **82** (2011)
Vietname	Tropical 15°C-34°C mid-May to mid-September	**30** (2002) **15** (2009)	**48** (1975)**79,7** (2002)**87,3** (2009) **South Vietname: 22** (1988)(20) **27** (1998) (21)	**389** (2002) **263** (2009)	**≈17** (1975) (24) **24** (2002) **28** (2009)

* *Source (unless otherwise specified):* **Population Reference Bureau, World Population Data Sheet** (4)
** *Source (unless otherwise specified):* **http://www.climate-zone.com/** (12)

It can be observed that those regions satisfy almost all the criteria (failing at maximum one), which allows a reliable comparison to Madeira. The exception is Vietnam, as it does not fulfill more than one of the requirements. Thus, this country was considered the "weakest" case, i.e., the least representative region in the study.

In *Table 2* is represented the dengue outbreaks' evolution along the past decades in the six selected countries.

Table:

2 Dengue outbreaks' history in the six selected countries

Dengue outbreaks								
Region	Year	Serotype	Duration	Frequency	Type	Number of cases	Attack rate (%)	Urban attack rate (%)
Cuba	1977(25)	DEN-1(32)	2 years(25)	–	Clinical (25)	477440 cases (1977)(25) 75692 (1979)(25)	5 0,77	7,5 1,2
	981(26)	DEN-2(26)	ND	2 years	Clinical (26)	344203(26)	3,4	5,1
	1997(26)	DEN-2(26)	ND	16 years	Laboratory-confirmed (26)	2946(26)	0,03	0,04
	2001(26)	DEN-3(26)	ND	1 year	Clinical (26)	11432(26)	0,1	0,14
	2002(26)	ND	ND	1 year	Clinical (26)	3011(26)	0,03	0,04
Guadeloupe	2001(27)	ND	ND	4 years	Clinical (27)	2400	0,6 (27)	1,4
	2005(27)	DEN-4(27)	4-6 months(27)	4 years	Clinical (27)	11500(27)	2,9	4,4
	2007(27)	DEN-2(27)	4-6 months(27)	2 years	Clinical (27)	19000(27)	4,8	6,1
	2009(28)	ND	Almost 1 year(28)	2 years	Clinical (28)	41100(28)	10	11,3

Dengue outbreaks								
Region	Year	Serotype	Duration	Frequency	Type	Number of cases	Attack rate (%)	Urban attack rate (%)
Puerto Rico	1963[25]	DEN-3[25]	1 year[25]	–	Laboratory-confirmed [25]	>27000[25]	1,2	2,5
	1972[25]	DEN-2[25]	1 year[25]	9 years	Clinical [25]	> 7000[25]	0,26	0,4
	1977[25]	DEN-1,2,3 [25]	ND	5 years	Clinical [25]	355000[25]	12,2	18,7
	1981[[26]	DEN-1[26]	2 years[26]	4 years	Clinical [26]	8350 (1981) 9536 (1982)[26]	0,28 0,32	0,4 0,5
	1986[26]	DEN-4[26]	ND	5 years	Clinical [26]	10659[26]	0,33	0,5
	1994[26]	DEN-2[26]	ND	8 years	Clinical [26]	22000[26]	0,63	0,76
	1997[26]	ND	ND	3 years	Clinical [26]	6955[26]	0,19	0,21
	1998[26]	ND	ND	1 years	Clinical [26]	17241[26]	0,47	0,5
	1999[26]	ND	ND	1 years	Clinical [26]	4993[26]	0,13	0,15
	2000[26]	ND	ND	1 years	Clinical [26]	2433[26]	0,06	0,07
	2001[26]	ND	ND	1 years	Clinical [26]	5233[26]	0,14	0,16
	2002[26]	ND	ND	1 years	Clinical [26]	1662[26]	0,04	0,06
Bahamas	1998[29]	DEN-1[29]	ND	–	Laboratory-confirmed [29]	365 [29]	0,15	0,18
	2003[29]	DEN-1[29]	ND	5 years	Laboratory-confirmed [29]	155[29]	0,05	0,06
	2011[29]	DEN-1[29]	ND	8 years	Laboratory-confirmed [29]	>3500[29]	0,88	1
Austrália*	1992[30]	DEN-2[30]	1 ano	–	Laboratory-confirmed [30]	≈20700	0,69[30]	0,78
	Past 5 years[30]	DEN-1,2,3 3[30]	ND	–	Laboratory-confirmed [30]	30-50 cases/ year[30]	0,001	0,002
Vietname**	1975[20]	ND	ND	–	Clinical [20]	19416[20]	0,11[20]	0,2
	1979[20]	ND	ND	4 years	Clinical [20]	21285[20]	0,12[20]	0,2
	1983[20]	ND	6 months[21]	4 years	Clinical [20]	77087[20]	0,38[20]	0,6
	1987[20]	DEN-2 DEN-3 [21]	6 months[21]	2 years	Clinical [20]	83905[20]	0,38[20]	0,55
	1988[20]	ND	ND	1 year	Clinical [20]	49237[20]	0,22[20]	0,3
	1992[20]	ND	ND	4 years	Clinical [20]	42363[20]	0,17[20]	0,93
	1997[21]	DEN-2[21]	6 months[21]	10 years	Clinical [21]	≈77000[21]	0,3	1,3
	1998[21]	DEN-3[21]	6 months[21]	1 year	Clinical [21]	119429[21]	0,44[21]	2
	2009 [21]	ND	1 year[21]	11 years	Clinical [31]	≈87300	0,1[31]	0,35

Values with grey color: Calculated manually taking into account the given information (formulas given in Methods)
*Specific area of Queensland ** Specific area of South Vietnam

On the general, the outbreaks lasted from 4 months to 2 years, with the most common duration period being from 4 to 6 months. Their frequency varied between 1 and 16 years, with the most common frequency being 2 years.

Cuba, with its first outbreak in 1977 and the last one in 2002, experienced *attack rates* from 0.03% (2002) to 5% (1977) and *urban attack rates* from 0.04% (2002) to 7.5% (1977). The cases were only confirmed in the laboratory in 1997, with an attack rate of 0.03% and an urban attack rate of 0.04%. This shows that the attack rate in Cuba decreased over time. In a different way, Guadeloupe had its major outbreaks from 2001 to 2009. The *attack rates*, regarding all clinical cases, varied from 0.6% (2001) to 10% (2009) and the *urban attack rates* varied from 1.4% (2001) to 11.3% (2009). Puerto Rico, on its turn, has many records of dengue. The first main one appeared in 1963 whilst the last main one was in 2002. The *attack rates* in this country varied from 0.04% (2002) to 12.2% (1977) and the *urban attack rates* varied from 0.06% (2002) to 18.7% (1977). The Bahamas and Australia-Queensland, on the other hand, presented their information in terms of laboratory-confirmed cases. The Bahamas had the lowest *attack rates*, varying from 0.05% (2003) to 0.88%

(2011). The corresponding *urban attack rates* varied from 0.06% (2003) to 1% (2011). According to the source, tourism was the responsible for the large attack rate increase in the outbreak of 2011 when compared to that of 2003[29]. Australia-Queensland experienced its first main dengue outbreak in 1992, with an attack rate of 0.69% and an urban attack rate of 0.78%. Since then, this region has had between 30 and 50 cases per year, which corresponds to an attack rate of 0.001%. Finally, South Vietnam experienced several outbreaks from 1975 to 2009. Specifically, the *attack rates*, all relative to clinical cases, varied from 0.1% (2009) to 0.44% (1998) and the *urban attack rates* varied from 0.2% (1975 and 1979) to 2% (1998).

Lastly, it was done an accurate analysis from all of the above information and studied all the *attack rates* and the *urban attack rates* for both clinical and laboratory-confirmed cases, whose corresponding mean, median and mode are shown in *Table 3.*

Table: 3 Analysis of the attack rates and the urban attack rates, for both clinical and laboratory-confirmed cases

	Clinical Cases		Laboratory-Confirmed cases	
	Attack rates	Urban attack rates	Attack rates	Urban attack rates
Mean	0,8	1,3	0,4	0,7
Median	0,29	0,5	0,15	0,18
Mode	0,1	0,5	–	–

The *attack rates* and the *urban attack rates* of Guadeloupe in 2009 (10% and 11.3%, respectively) and Puerto Rico in 1977 (12.2% and 18.7%, respectively) were excluded from the above calculation because they were considered outliers. An external factor could have been the cause for these uncommon *attack rates* for Guadeloupe and Puerto Rico, since these extreme values only appear in one year.

From this table, it can be concluded that the dengue *attack rates* in Madeira were expected to be approximately from 0.8% to 1.3% (*urban population*), for clinical cases, and from around 0.4% (*urban population*) to 0.7%, for confirmed cases. Applying this attack rate to the population of 0.27 million living in Madeira Island, and taking into account that 0.19 million is *urban population*, a number between **2160 and 2470 for dengue clinical cases and between 760 and 1890 for dengue laboratory-confirmed** cases were expected.

4

Discussion/Conclusion

In the archipelago of Madeira were diagnosed 2164 clinical cases until the 3rd of February of 2013. Since Madeira's rainy months are from November to February, this number is not likely to increase significantly for the rest of the year. In this study it was estimated a number between 2160 and 2470 dengue clinical cases to occur in 2013 so, for the moment, available data seems to be in close support of these results.

There was no reference to any connection between attack rates and frequency of outbreaks.

It can also be discussed the extension in which Madeira should be compared with the selected regions in terms of other indicators besides the climate and the level of development. Even so, the level of development was considered a very important indicator because it is a crucial factor for the spread of the disease. It is known that developed countries typically divulge more information to their citizens and also have better means to fight diseases. The *infant mortality* rate is also generally considered a good measure of the population health[33] and, hence, is a good measure of the level of development of a country. Furthermore, the percentage of *urban population* and *population density* are also related to the spread of dengue, as urbanized and highly populated zones are the best places for the mosquitoes to thrive.

Tourism may be another factor influencing the spread of dengue because travelers can be good vectors of various diseases. When this factor was analyzed in the six chosen regions[34], it was concluded that Guadeloupe, Puerto Rico and The Bahamas were the most similar to Madeira. The mean *attack rates* for these regions were calculated again and similar results to the ones before were obtained. Thus, analyze the dengue history related to tourism does not add much information to the above study.

In addition, this analysis is subjective because the information about dengue past episodes in other countries is being studied and used to anticipate its intensity in Madeira and each country reacts to an outbreak in a different way. However, stressing that the goal of this study was not to get exact numbers of dengue cases in 2013, but to find some boundaries for them, it proves to be adequate. In fact, the prediction of the exact number of cases is unrealistic and the presentation of an estimate is the most useful tool for the Portuguese health institutions to help in the design of a mitigation plan and take action.

This work is just a simple and initial useful approach. Deeper and more complex analysis must be performed as the definitive information of this dengue epidemic in Madeira (2013) becomes gradually available.

5

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